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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,666	12/13/2004	Michal Eisenbach-Schwartz	EIS-Schwartz37	7353

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BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
KOLKER, DANIEL E	
ART UNIT	PAPER NUMBER
1649	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,666	EISENBACH-SCHWARTZ ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-39* is/are pending in the application.

4a) Of the above claim(s) *38 and 39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *23-39* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/18/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks filed 20 February 2007 have been entered. Claims 23 – 39 are pending.

Election/Restrictions

2. Applicant's election of Group 1 (claims 23 – 27, each in part, drawn to administration of cells that have been pulsed with a NS-specific antigen or an analog thereof) in the reply filed on 20 February 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 38 – 39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 20 February 2007.

4. Claims 23 – 37 are under examination to the extent they read on administration of cells that have been pulsed with a NS-specific antigen or an analog thereof.

Claim Objections

5. Claims 23 – 37 are objected to because of the following informalities: they recite or encompass non-elected subject matter, particularly administration of copylmers and non-self antigens as recited in claim 23 parts (c) and (d), claim 31 parts (c) and (d), and claim 37, parts (c) and (d) for example.

Claim 34 has a grammatical error; it ends with a comma instead of a period

Claim 35 has a spelling error; the word "sistemically" should be "systemically". Claim 35 also has a grammatical error; it does not end with a period.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23 – 37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for administration of dendritic cells pulsed with residues 87 –

99 of myelin basic protein or the same peptide wherein the lysine at residue 91 was replaced with alanine and subsequent attenuation of locomotor symptoms in patients with spinal cord injury, does not reasonably provide enablement for:

- administration of cells pulsed with any and all NS-specific antigen or analog or derivative thereof as broadly claimed in independent claims 23, 31, and 36, or for
- prevention of neuronal degeneration as set forth in claim 23, or for
- treatment of all diseases or conditions as recited in claim 31
- treatment of the specific diseases and conditions recited in claims 32 – 33.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (FED. Cir. 1988).

Here, the nature of the invention, treatment of spinal cord injury in particular (i.e. claims 31 and 36) or inhibiting neuronal degeneration or promoting nerve regeneration (claim 23), or treating an injury, disorder, or disease (claim 31) by administration of cells from the immune system, is complex. The art recognizes that spinal cord injury is difficult to treat and involves interactions of several physiological processes, including inflammatory responses, immune reactions, formation of scar tissue, and growth of axons. Whether or not a treatment will be effective is complex and unpredictable. See for example Yoles et al. (2001. Journal of Neuroscience 21:3740-3748), who teach that spinal cord injury is characterized by a period of initial damage and injury, followed by secondary cell loss which affects neurons that had survived the initial trauma. Yoles also teaches that certain agents, for example steroids and anti-inflammatory cytokines, are either beneficial or harmful to the injury depending on when they are administered. Thus this is a complex field in which it is difficult to extrapolate from specific findings as to therapeutic efficacy of compounds to more general conclusions about related compounds or even to different dosing and treatment regimens.

What is actually enabled by the specification is relatively narrow. The specification discloses, beginning at p. 23, the results of experiments in which rats that received dendritic cells (DCs, which are a type of antigen-presenting cells) that had been pulsed with either a) a peptide consisting of residues 87 – 99 of myelin basic protein (called MBP 87 – 99) or b) or the same peptide wherein the lysine at residue 91 was replaced with alanine (called A91) monitored for recovery from spinal cord injury. As spinal cord injury is specifically recited in claims 31 and 36, this finding is on point to those claims. The specification discloses that when animals received spinal cord injures and were subsequently treated with dendritic cells pulsed with these antigens, the animals showed significant recovery of locomotor function as determined by the Basso, Beattie, and Besnahan (BBB) scale (see for example p. 31 final paragraph). Thus the specification is enabling for improving locomotor deficits following spinal cord injury by administering dendritic cells pulsed with either MBP 87 – 99 or A91.

However, what is claimed is considerably broader than what is disclosed, is not enabled by the specification, and could not be enabled by the skilled artisan in the absence of undue experimentation. The claims as written encompass treatment by administration of antigen-presenting cells that have been pulsed with any nervous-system specific antigen or analog or derivative thereof. What has been demonstrated is treatment by administration of dendritic cells pulsed with a single antigen (MBP 87 – 99) or a single variant thereof (A91, which is the protein of SEQ ID NO:4 recited in claim 37). The prior art recognized that another part of MBP, specifically residues 68 – 86, also has the same effect. Huang et al. (2000. Clin Exp Immunol 122:437-444, reference AE on IDS filed 18 August 2005) teach inducing tolerance to EAE in rats treated with dendritic cells pulses with MBP 68 – 86. However, the reference clearly shows that administering dendritic cells pulsed with other nervous-system specific antigens is not successful in this same paradigm. See Huang, p. 443 first complete paragraph which teaches that "DC pulsed in vitro with ... MOG peptide 35 – 55 of PLP peptide 139 – 151 did not suppress the development of EAE" in rats. Thus even though MOG (myelin oligodendrocyte glycoprotein) and PLP (proteolipid protein) are constituents of myelin as is MBP, they are not effective in preventing or inhibiting this form of neuronal degeneration. Clearly, the only antigen that is successful in such a paradigm is MBP itself. Even other myelin proteins are not effective. At page 17, the specification discusses several proteins which may be effective and includes Nogo protein and neurotransmitter receptors, among others. The proteins listed share no common core sequence with MBP, and do not have common functions. Even other proteins derived from

myelin are not effective in treating or preventing disease. As the specification offers only two working examples of ameliorating symptoms by administering cells pulsed with nervous-system specific antigens, the prior art indicates other nervous-system specific antigens will not work, and the specification offers no guidance as to how to overcome this finding, the claimed methods are not enabled over the full scope of nervous-system specific antigens as recited in claims 23, 31, and 36; note the definition of nervous-system specific antigens on p. 17 of the specification clearly is inclusive of any and all such antigens, independent of their structure. All claims under examination, with the exception of claim 37 which is limited to a single antigen, encompass administration of cells pulsed with any antigen. The specification provides only two working examples of this, one with part of MBP and one with a peptide that differs from an MBP fragment by a single amino acid. Thus given the state of the art and what is actually disclosed in the specification, the skilled artisan would have to resort to undue experimentation in order to make and use the invention commensurate in scope with the claims.

Additionally, the specification does not reasonably provide enablement for prevention of neuronal degeneration as recited in claim 23. The prior art indicates that all subjects undergo neuronal degeneration as a part of the normal aging process. Bussiere et al. (2001. Morphological Changes in Human Cerebral Cortex During Normal Aging. In Hof et al. Funtional Neurobiology of Aging. San Diego: Academic Press, pp. 77 – 84) teach that the hilus and subiculum are particularly vulnerable to neural loss, and that such degeneration is essentially indistinguishable between normal humans and those with Alzheimer's disease (see for example Figure 7.4). Bussiere also discusses the neural loss that affects all patients (see abstract and p. 78, part B). There is no indication that this is preventable, and such neural loss is generally to be considered a normal part of the aging process. The specification provides no evidence of prevention of neuronal degeneration, and provides no guidance to the artisan as to how to accomplish prevention of neuronal degeneration. Given that such is generally considered impossible, as evidenced by the Bussiere reference, and the specification sets forth neither working nor prophetic examples of prevention and offers no guidance as to how to achieve it, it would take undue experimentation for the skilled artisan to prevent neuronal degeneration as claimed.

Finally, the specification does not reasonably provide enablement for treatment of all diseases as encompassed by claim 31 and as recited in claims 32 – 33. Claim 31 is not limited to those diseases and conditions recited in dependent claims 32 – 33, and necessarily is

broader. Even if, for the sake of argument, the specification had provided enablement for every disease recited in claims 32 – 33, it would not be enabling for all diseases, disorders, or injuries of the CNS or PNS as recited in claim 31. For example major depression is certainly a disorder of the PNS, but it is thought to be due to an imbalance of neurotransmitters such as serotonin, not to death of neurons by crushing.

The specification shows functional recovery of locomotor activity by administration of MBP-pulsed dendritic cells to animals that have a spinal cord injury. However, there is no reasonable expectation that this success would be therapeutic for epilepsy, which is caused by excessive neural firing, or in treatment of Parkinson's disease, which is caused by death of dopaminergic neurons in the substantia nigra, or for depression. There is no reason to believe that the treatments would be useful in treatment of the diseases in claim 32, as they do not share a common mechanism of action. Spinal cord injury is quite different from hemorrhagic stroke, as the former is caused by a crushing injury whereas the latter is caused by excessive bleeding in the brain. The diseases and conditions encompassed by claim 31 and recited in claims 32 – 33 do not share a common mechanism of action or etiology with spinal cord injury, thus the skilled artisan would not expect that such diseases could be treated by those therapies shown to be effective in promoting recovery of locomotor function in spinal cord injury.

Given the complex nature of the invention, breadth of the claims, the lack of working examples commensurate in scope with the claims, the state of the prior art which demonstrates that many of the embodiments encompassed in the claims would not work, and the lack of guidance as to how to overcome these established obstacles, the skilled artisan would not be able to practice the full scope of the claimed invention in the absence of resorting to undue experimentation.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 23 – 28, 31 – 34, and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Eisenbach-Schwartz (U.S. Patent 5,800,812, cited on IDS filed 18 August 2005).

Eisenbach-Schwartz teaches obtaining antigen-presenting cells, including dendritic cells and culturing them in the presence of nerve segments, which reasonably meets the limitation of "a nervous-system specific antigen" as recited in claims 23, 31, and 36 (see column 3 lines 35 – 60). Note the culturing is performed for a limited period of time before administration and thus is reasonably a pulse as recited in claims 23, 31, and 36; see particularly column 7 lines 28 - 32 which recites times such as 2 – 24 hrs for the pulse. Eisenbach-Schwartz teaches administering these cells to patients in need of treatment, including human subjects with spinal cord damage (see column 9 second paragraph for recitation of human subjects and lines 27 – 35 for recitation of spinal cord injury). Thus the reference anticipates independent claims 23, 31, and 36.

Claims 24 – 27 are rejected as Eisenbach-Schwartz teaches autologous dendritic cells can be used for treatment of humans (see column 5 lines 55 – 63 for autologous cells and column 9 second paragraph for treatment of humans). Note that the dendritic cells can be obtained from those tissues recited in claim 27 (see '812 patent column 5 lines 55 – 63). Claim 28 is rejected as the reference teaches adding several of the recited biologically active agents listed (see '812 patent, column 7 lines 16 – 25). Claims 32 – 33 are rejected as the reference teaches treatment of spinal cord injury and glaucoma among others (column 9 lines 30 – 35). Claim 34 is rejected as the patent teaches local administration (column 9 lines 5 – 10).

8. Claims 23 – 28, 31 – 34, and 36 are rejected under 35 U.S.C. 102(a) and under 35 USC 102(e) as being anticipated by Eisenbach-Schwartz (U.S. Patent 6,267,955, issued 31 July 2001, filed 11 March 1998, cited on IDS filed 18 August 2005). Note the reference qualifies as prior art under both § 102(a) and § 102(e).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37

CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Note that even if applicant is able to overcome the rejection under 102(e) as described in the previous paragraph, the reference still qualifies as prior art under 102(a) as it in by another and was published before the earliest effective filing date of this application.

Eisenbach-Schwartz teaches obtaining antigen-presenting cells, including dendritic cells and culturing them in the presence of nerve segments, which reasonably meets the limitation of "a nervous-system specific antigen" as recited in claims 23, 31, and 36 (see column 2 lines 49 – 67). Note the culturing is performed for a limited period of time before administration and thus is reasonably a pulse as recited in claims 23, 31, and 36; see particularly column 8 first complete paragraph which recites times such as 2 – 24 hrs for the pulse. Eisenbach-Schwartz teaches administering these cells to patients in need of treatment, including human subjects with spinal cord damage (see column 9 lines 55 – 60 for recitation of human subjects and column 10 lines 54 – 56 for recitation of spinal cord injury). Thus the reference anticipates independent claims 23, 31, and 36.

Claims 24 – 27 are rejected as Eisenbach-Schwartz teaches autologous dendritic cells can be used for treatment of humans (see column 2 lines 52 – 53 for autologous cells and column 9 lines 55 – 57 for treatment of humans). Note that the dendritic cells can be obtained from those tissues recited in claim 27 (see '955 patent column 6 second paragraph). Claim 28 is rejected as the reference teaches adding several of the recited biologically active agents listed (see '955 patent, column 7 lines 47 – 65). Claims 32 – 33 are rejected as the reference teaches treatment of spinal cord injury and glaucoma among others (column 10 final paragraph). Claim 34 is rejected as the '955 patent teaches local administration (column 9 lines 55 – 64).

9. Claims 23 and 28 – 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Huang (2000. Clin Exp Immunol 122:437-444, reference AE on IDS filed 18 August 2005).

Huang teaches pulsing dendritic cells, which are antigen presenting cells, with myelin basic protein peptide 68 – 86, which is a peptide derived from a NS-specific antigen as recited in claim 23. Huang teaches administration of the dendritic cells to patients (rats), which induces protection against subsequent induction of EAE, which is a degenerative disease. The rats are reasonably individuals in need of inhibition of neuronal degeneration, as they will later receive a

treatment that induces a neurodegenerative disease. It is reasonable that rats are included within the scope of the invention, as the specification presents data from rats and indicates that the data are illustrative of the invention (see p. 23 lines 21 – 30). Note there is no particular definition of the "individual in need", as recited in claim 23, which is limited to humans. Thus the reference fairly teaches inhibiting neuronal degeneration as recited in claim 23. Claims 28 – 29 are rejected as Huang teaches culturing the dendritic cells in medium comprising both IL-4 and GM-CSF (see p. 438 second paragraph).

10. Claims 23, 28, 31, and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Ben-Nun et al. (1990. European Journal of Immunology 20:357 – 361).

Ben-Nun teaches pulsing antigen-presenting cells, specifically macrophages, with MBP and subsequent administration to mice that had already had EAE induced. See p. 357 – 358 (sections 2.1 – 2.2) for a description of the procedure. Ben-Nun teaches that the procedure is sufficient to attenuate the development of EAE (see paragraph spanning pp. 358 – 359). Thus as the reference teaches administration of the antigen-presenting cells that had been pulsed with MBP, a NS-specific antigen, and subsequent attenuation of severity of symptoms of EAE, it fairly anticipates independent claims 23 and 31. Claim 28 is rejected as Ben-Nun teaches culturing the antigen-presenting cells in the presence of IFN-gamma (see p. 358 first complete paragraph). Claim 35 is rejected as the reference teaches intraperitoneal administration is sufficient to treat the disease.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 23, 28, 31 – 32, and 34 – 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ben-Nun et al. (1990. European Journal of Immunology 20:357 – 361) in view of Hauben (2000. The Lancet 354:286-287), Popovich (1996. Journal of Neuroscience Research 45:349-366), and Schwartz (2001. Trends in Molecular Medicine 7:252-258).

The reasons why claims 23, 28, 31, and 35 are anticipated by Ben-Nun et al. are set forth in the rejection under 35 USC 102 above. Briefly Ben-Nun teaches treatment of a disease, specifically EAE, by administration of antigen-presenting cells (which present their antigen to T cells) that have been pulsed with the NS-specific antigen MBP. However Ben-Nun does not teach treatment of spinal cord injury as recited in claims 32 and 36 or local administration as recited in claim 34.

Hauben teaches treatment of spinal cord injury, as recited in claims 32 and 36, by administration of T cells that recognize the NS-specific antigen MBP, which is on point to independent claims 23, 31, and 36. The reference teaches that systemic administration of the T cells is sufficient to improve the locomotor activity of rats that have spinal cord injury, and that the degree of improvement is considerably greater than animals that received either PBS or T-cells that recognize ovalbumin. However Hauben does not teach administration of antigen presenting cells as recited in claims 23, 31, and 36.

Popovich teaches the similar natures and mechanisms of EAE and spinal cord injury. Both are characterized by immune responses, inflammation, and demyleination. In both cases, patients suffer from motor deficits. See particularly abstract, Table 1 on p. 351. The reference teaches that since autoimmune diseases such as EAE and traumatic injury such as spinal cord injury share similar symptoms and underlying mechanisms, treatments known to be effective for the former should be tried again in the latter (see p. 360). However Popovich does not teach treatment of spinal cord injury by administration of antigen-presenting cells.

Schwartz teaches the concept of "protective autoimmunity" for treatment of multiple diseases and conditions of the CNS including spinal cord injury as recited in claims 32 and 36. Schwartz teaches that the presence of T cells reactive against NS-specific antigens in the central nervous system is not a sign of illness or infection, but rather a therapeutic mechanism by which the immune system attenuates disease (see p. 255, "Protective autoimmunity as a

mechanism for homeostasis in the CNS"). Schwartz teaches that the CNS is immunologically privileged; that is, immune system activity is attenuated or completely absent (end of p. 252). Thus Schwartz provides the motivation to the artisan of ordinary skill to increase the activity of the immune system within the CNS, for example by local administration as recited in claim 34 or systemic administration as recited in claim 35.

It would have been obvious to one of ordinary skill in the art to administer antigen-presenting cells that have been pulsed with MBP, as taught by Ben-Nun, for treatment of spinal cord injury. The motivation to do so would be to treat patients with spinal cord injury. It would be reasonable to expect success; such expectation comes directly from the prior art references themselves. While the reference by Hauben teaches administration of T cells rather than antigen-presenting cells, since antigen-presenting cells in fact present their antigens to T cells, it would have been obvious to substitute the APCs for the T cells. The motivation to make such a substitution is provided by Schwartz, who teaches that the CNS is immunologically privileged, so it would need APCs to be administered locally. Popovich further provides a reasonable expectation of success as the reference teaches the symptoms and mechanisms underlying EAE and spinal cord injury are similar, thereby providing the expectation that treatments for the former (i.e. as taught by Ben-Nun) will be successful in patients with spinal cord injury.

12. Claims 23, 28, 31 – 32, and 34 – 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ben-Nun in view of Hauben, Popovich, and Scwartz as applied to claims 23, 28, 31 – 32, and 34 – 36 above, and further in view of Gaur (1997. Journal of Neuroimmunology 74:149 – 158).

The reasons why claims 23, 28, 31 – 32, and 34 – 36 are obvious are set forth in the previous rejection. However none of the cited references teach the protein of SEQ ID NO:4 as recited in claim 37.

Gaur teaches the protein of SEQ ID NO:4. It is referred to as "A91" and is residues 87 – 99 of MBP, with a K to A substitution at residue 91 (see p. 150 section 2.2). The peptide, when administered to animals with EAE, ameliorates the symptoms of the disease (p. 152, section 3.2). Furthermore, the peptide stimulates cytokine production by the MBP-reactive T-cells (see for example Figure 5 and section 3.4). However Gaur does not teach administration of antigen-presenting cells that have been pulsed with this peptide.

It would have been obvious to one of ordinary skill in the art to pulse the antigen presenting cells with the protein of SEQ ID NO:4 (i.e. A91, taught by Gaur) prior to administration for treatment of spinal cord injury. The motivation to do so would be to effectively treat spinal cord injury. While Gaur is on point to treatment of EAE and not spinal cord injury, the reference by Popovich indicate that the two diseases share mechanisms and symptoms, and Schwartz teaches that increasing the activity of the immune system, (e.g. by increasing T cell activity as shown in Gaur's Figure 5) is therapeutic in these sorts of conditions.

13. Claims 23 – 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huang (2000. Clin Exp Immunol 122:437-444, reference AE on IDS filed 18 August 2005) in view of Link (2001. Journal of Neuroimmunology 114:1-7).

The reasons why Huang anticipates claims 23 and 28 – 29 are set forth in the rejection under 35 USC § 102 above. However the reference does not teach administration of human dendritic cells, autologous to the patient in need, obtained from skin, spleen, thymus, marrow, lymph nodes, or peripheral blood as encompassed by claims 24 – 27.

Link teaches administration of autologous dendritic cells that have been "exposed to a selected biological milieu in vitro" and then returning the cells to the same patient (see section 4, beginning at the bottom of p. 3). Link teaches that this sort of therapy will be useful for treatment of human autoimmune diseases such as multiple sclerosis, which is the human correlate of EAE. While claim 27 recites product-by-process limitations as to where the dendritic cells may be obtained, it is noted that Link teaches dendritic cells from spleen are sufficient (p. 4, first complete paragraph). Thus Link teaches administration of autologous dendritic cells to patients in need, where the cells are obtained from spleen, and therefore is on point to the limitations of claims 24 – 27. However Link does not explicitly teach the administration of these cells to human patients.

It would have been obvious to one of ordinary skill in the art to modify the method of Huang to use autologous dendritic cells to treat human patients, as suggested by Link, with a reasonable expectation of success. The motivation to do so would be to reduce the possibility of immune rejection of transplanted cells. If the cells injected into the patient are autologous (i.e., from that patient), they will not be recognized as foreign and thus there will be no need for the use of immunosuppressant drugs. It would be reasonable to expect success when combining the teachings of the two references, as both are on point to treatment of autoimmune

neurodegenerative diseases (MS and EAE) by administration of antigen-presenting cells that have been exposed to a particular set of biological molecules *in vitro*.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 23 – 28, 31 – 34, and 36 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 – 3, 6 – 28, 31 – 34, and 37 – 46 of U.S. Patent No. 6,267,955. Although the conflicting claims are not identical, they are not patentably distinct from each other because in each case the claims are drawn to methods of administering antigen-presenting cells that have been pulsed nervous-system specific antigens for treatment of diseases including those disease characterized by axonal damage.

15. Claims 23 – 28, 31 – 34, and 36 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 – 26 of U.S. Patent No. 5,800,812. Although the conflicting claims are not identical, they are not patentably distinct from each other because in each case the claims are drawn to methods of administering antigen-presenting cells that have been pulsed nervous-system specific antigens for treatment of diseases including those disease characterized by axonal damage.

Inventorship

16. Claims 23 – 28, 31 – 34, and 36 are directed to an invention not patentably distinct from claims 1 – 3, 6 – 28, 31 – 34, and 37 – 46 of commonly assigned patent 6,267,955 and claims 1 – 26 of commonly assigned patent 5,800,812 as explained in the double-patenting rejection above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned 6,267,955 and 5,800,812, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Conclusion

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

DK

Daniel E. Kolker, Ph.D.
April 24, 2007

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER